(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau

(43) International Publication Date
8 May 2003 (08.05.2003)

PCT

(10) International Publication Number
WO 03/037084 A1

(51) International Patent Classification[7]: A01N 25/02, 43/653, 43/54, 43/40

(21) International Application Number: PCT/GB02/04656

(22) International Filing Date: 15 October 2002 (15.10.2002)

(25) Filing Language: English

(26) Publication Language: English

(30) Priority Data:
0126144.5 31 October 2001 (31.10.2001) GB

(71) Applicant *(for all designated States except US)*: **SYNGENTA LIMITED** [GB/GB]; European Regional Centre, Priestley Road, Surrey Research Park, Guildforf, Surrey GU2 7YH (GB).

(72) Inventor; and
(75) Inventor/Applicant *(for US only)*: **WARRINGTON, Roger, Paul** [GB/GB]; Jealott's Hill International Research Centre, Bracknell, Berkshire RG42 6YA (GB).

(74) Agents: **HOUGHTON, Malcolm, John** et al.; Intellectual Property Department, Syngenta Limited, P.O. Box 3538, Jealott's Hill Reasearch Centre, Bracknell RG42 6YA (GB).

(81) Designated States *(national)*: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW.

(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

Published:
— *with international search report*
before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments

For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

WO 03/037084 A1

(54) Title: PESTICIDAL FORMULATIONS

(57) Abstract: A concentrated pesticidal solution is provided which comprises one or more water-insoluble pesticides (usually 0.5-50% w/v) and lignin (suitably in the weight ratio of 1:10 to 1:1 of lignin to pesticide) dissolved in a water miscible, polar solvent, preferably *N-methyl* pyrrolidone. The solutions are particularly useful in providing storage stable soluble concentrates of certain strobilurin fungicides.

PESTICIDAL FORMULATIONS

This invention relates to pesticidal formulations and more particularly to concentrated solutions of water-insoluble pesticides. It also relates to the preparation of these concentrated solutions and their uses in water diluted form.

Pesticides which have a low solubility in water and which are chemically stable in water are commonly marketed in the form of aqueous suspension concentrates (SCs) and diluted for use in the field. The suspended pesticidally active ingredient needs to have a small particle size in order keep it suspended while stored as a concentrate and when diluted further with water. This normally requires the active ingredient to be milled, which can be time consuming and costly. Even so, problems are often encountered with suspension concentrates as a result of settling during prolonged storage, the resistance of settled particles to re-suspension and sometimes an increase in particle size of the active ingredient during storage.

One alternative is to dissolve the water-insoluble active ingredient in a water immiscible solvent, such as an aromatic hydrocarbon, to form an emulsifiable concentrate (EC). This can be stored as a stable solution and diluted with water when ready for use to form a milky emulsion of small particle size. Water-insoluble pesticides that are not readily soluble in the normal water-insoluble solvents may be dissolved in a water miscible solvent to form a storage stable soluble concentrate (SL). The pesticide forms a suspension on dilution with water. Soluble concentrates of this kind are described in, for example, WO 92/10937. These SLs are three component formulations in which a solid water insoluble pesticide and a dispersant are solubilised in a water miscible solvent. A range of dispersants are mentioned including alkylated vinylpyrrolidone polymers, ethylene oxide propylene oxide/propylene glycol condensates, nonylphenol ethylene oxide adducts, and various ethoxylates. The solvents include acetonitrile, α-butyrolactone, dimethyl ketone, dimethylfuran, dimethyl sulphoxide, methanol and *N*-methyl pyrrolidone.

The drawback in using water-soluble solvents for dissolving active ingredients of low water solubility is their poor dilution properties in water. The active ingredient is often rapidly precipitated as coarse crystals giving both application problems, such as spray filter or nozzle blockage, and poor or inconsistent bioefficacy. To prevent, or, more usually, delay precipitation, an excess of emulsifying or dispersing agent, typically at a 1:1 ratio with the

active ingredient, needs to be incorporated and at these concentrations surfactants may give rise to phytotoxicity problems in their own right.

According to the present invention, there is provided a concentrated pesticidal solution which comprises one or more water-insoluble pesticides and lignin dissolved in a water miscible, polar solvent.

The pesticide or pesticides used in the solution concentrate of the invention are water insoluble and may be solid or liquid, but the invention is of particular value for pesticides that are solid at ambient temperature. Normally they will have a solubility in water of not more than 0.2% w/v. They must also be soluble in the chosen water miscible, polar solvent.

The amount of pesticide or pesticides used will usually be from 0.5 to 50% w/v, more usually from 1 to 30% w/v, and typically from 5 to 20% w/v, of the total solution.

Pesticides include herbicides, insecticides and fungicides. The invention is particularly suitable for any pesticide or mixture of pesticides having a solubility in water of not more than 0.2% w/v. Examples of pesticides for use in this invention are napropamide, haloxyfop, clodinafop-propargyl, mesotrione, cypermethrin, alpha-cypermethrin, beta-cypermethrin, cyproconazole, difenoconazole, hexaconazole, penconazole, tebuconazole, azoxystrobin, picoxystrobin, kresoxim-methyl, metominostrobin, picoxystrobin, pyraclostrobin, trifloxystrobin, cyprodinil, metalaxyl, mefenoxam, fluazinam, fludioxonil, paclobutrazol, thiabendazole and quinoxyfen. The invention is, however, particularly useful for fungicides, especially for triazole fungicides and strobilurin fungicides and for fungicidal mixtures, especially mixtures of a strobilurin fungicide, for example picoxystrobin, with a triazole fungicide such as hexaconazole or cyproconazole. Of particular interest are solution concentrates made from a fungicide selected from the group consisting of azoxystrobin, picoxystrobin, tebuconazole, cyproconazole, and picoxystrobin in admixture with cyproconazole.

By lignin is meant a lignin in its free acid state, and not an alkali metal salt of lignin, such as the sodium salt, or a lignosulphonate. Lignin, which is a phenyl propene polymer of variable molecular weight, may be obtained from the spent liquors of the sulphate and soda processes used in the wood pulping industry. A lignin so obtained is known as an alkali lignin and further designated a sulphate (or kraft) lignin or a soda lignin. Of particular suitability for use in the present invention is Indulin AT (Indulin AT is a trade name), which

is a highly purified lignin made from pinewood-sulphate black liquor and produced in the form of a free flowing brown powder.

The amount of lignin used in the solution concentrate of the present invention in relation to the amount of pesticide used is suitably in the weight ratio of from 1:10 to 1:1, usually from 1:8 to 1:2, preferably from 1:6 to 1:4, and typically 1:5, of lignin to total pesticide.

Any water miscible polar solvent that can dissolve both the pesticide and lignin may be used in the invention. Suitable solvents include γ-butyrolactone, tetrahydrofurfuryl alcohol, *N*-methyl pyrrolidone, dimethyl sulphoxide, *N,N*-dimethylformamide and ethyl lactate. Preferred solvents are γ-butyrolactone and tetrahydrofurfuryl alcohol, and a particularly preferred solvent is *N*-methyl pyrrolidone. Mixtures of polar solvents may also be used, for example, a 50:50 mixture of *N*-methyl pyrrolidone and poly(ethylene glycol) 200. The amount of solvent used is sufficient to bring the total solution to 100% w/v.

Although not essential, the solution concentrate may include other additives, for instance, polymer stabilisers or anti-settling agents to improve dilution. Examples of suitable stabilisers or anti-settling agents include water soluble and water insoluble polymers such as ethyl cellulose, casein, hydroxy propyl cellulose, *Avicel*™ CL-611 (based on microcrystalline cellulose), *Agrimer*™ VEMA AN-216 (a vinylether maleic anhydride copolymer, MW 55,000 to 80,000), NU-FILM-P™ (poly-1-p-menthene) and *Kelzan*™ (a xanthan gum). Such additives are conveniently used in amounts up to 0.5% w/v, for example 0.1 to 0.4% w/v, typically 0.25% w/v, of the total formulation, depending on their solubility in the polar solvent used. For instance, the maximum amount of *Avicel* CL-611 and *Kelzan* that can be dissolved in a *N*-methyl pyrrolidone based concentrate is about 0.1% w/v.

In one embodiment the invention provides a concentrated pesticidal solution which comprises:

(a) from 1 to 30% w/v, usually from 5 to 30% w/v and typically from 10 to 20% w/v, of one or more water insoluble pesticides and

(b) lignin in the weight ratio of from 1:10 to 1:1, usually from 1:8 to 1:2 and preferably from 1:6 to 1:4, typically 1:5, of component (a), both (a) and (b) being dissolved in

(c) a water miscible, polar solvent, such as γ-butyrolactone, tetrahydrofurfuryl alcohol, ethyl lactate and, preferably, *N*-methyl pyrrolidone.

In this embodiment, the concentrated solution optionally contains up to 0.5% w/v of other additives, such as a stabiliser or antisettling agent like ethyl cellulose.

The concentrated solution of the invention is prepared by dissolving the pesticide or pesticides, the lignin and, optionally, a stabiliser or other additive in the polar solvent. The ingredients may be added to the solvent in any order. Usually this is done at ambient temperature with suitable agitation or stirring. To assist dissolution, the solvent may be heated to temperatures up to, for example, 50°C.

When ready for use, the concentrated solution is diluted with water, usually by adding the solution to a stirred volume of water to give an aqueous dispersion of the pesticide or pesticides containing, for example, from 0.0001 to 1% w/v of the pesticide or pesticides. The aqueous pesticidal solution is then applied by spraying, or by any other known technique, to the location requiring treatment.

Thus, in a further embodiment of the present invention, there is provided a method of combating or controlling an agricultural pest which comprises applying to the pest or to a locus of the pest a pesticidally effective amount of an aqueous dispersion prepared by dispersing in water a concentrated pesticidal solution according to the invention.

The advantage of the concentrated pesticidal solutions of the present invention is that they can produce sub-micron (ca. 0.4μm) essentially mono-disperse particles on dilution into water which are stable to subsequent growth for at least 24 hours.

The invention is illustrated with reference to the following Examples. In the Examples the following abbreviations are used:

ai	= active ingredient	SL	= soluble concentrate
ppm	= parts per million	w/v	= weight/volume
w/w	= weight/weight	init	= initial
NMP	= *N*-methylpyrrolidone	GBL	= γ-butyrolactone
DMSO	= dimethylsulphoxide	THFA	= tetrahydrofurfuryl alcohol

PEG 200 = poly(ethylene glycol), average molecular weight 200

EL = ethyl lactate

EXAMPLE 1

This Example shows how the particle size is assessed when various concentrated pesticidal solutions, prepared according to the present invention, are diluted in water. Results are given for a number of invention solutions.

Method of Dispersion Testing

Formulations were tested for dispersing properties in water by adding 2.5ml solution concentrate by pipette to a stoppered Crow receiver containing 97.5ml of a CIPAC standard hard water. The initial "bloom" was noted when the first few drops were added to the water, then the receiver was inverted 3 times and homogeneity of the dispersion was noted. Checks were made at set time intervals over a 24 hour period to check for any sedimentation or crystallisation.

Particle size checks on dilutions initially and after 24 hours were carried out using a Malvern Mastersizer S. Instrument parameters were as follows:

Polydisperse model	Particle size values quoted:-
Obscuration 2-4%	volume median diameter D(v,0.5)
Pump speed 40%	volume mean diameter D[4,3]
Stirrer Speed 20%	% less than 1 μm
Ultrasonics – nil	

The CIPAC standard hard water types that were used were CIPAC A and CIPAC C. These have the following characteristics:

CIPAC A: 20 ppm hardness; pH 5.0-6.0; Ca^{2+} : Mg^{2+} = 1:1

CIPAC C: 500 ppm hardness; pH 7.0-8.0; Ca^{2+} : Mg^{2+} = 4:1

(a) Soluble concentrates of azoxystrobin

SL formulations containing 10% w/v azoxystrobin in NMP and varying levels of lignin were prepared and tested for dilution properties. Tables 1 and 2 below show the results.

Table 1: Azoxystrobin dilutions in CIPAC A water

Indulin AT % w/v	Initial CIPAC A			24 hour CIPAC A		
	Mean	Median	%<1 µm	Mean	Median	%<1 µm
1	9.71	0.44	85.69	0.39	0.37	100.00
2	3.46	0.38	90.56	1.25	0.39	95.68
3	0.40	0.38	100.00	0.39	0.37	100.00
5	0.39	0.37	100.00	0.38	0.36	100.00
10	2.77	0.38	76.31	4.51	0.41	70.43

Table 2: Azoxystrobin dilutions in CIPAC C water

Indulin AT % w/v	Initial CIPAC C			24 hour CIPAC C		
	Mean	Median	%<1 µm	Mean	Median	%<1 µm
1	-	-	-	0.88	0.38	94.11
2	1.39	0.37	88.05	0.53	0.39	96.58
3	0.74	0.38	93.62	1.96	0.41	83.11
5	1.33	0.40	87.76	85.44	0.61	64.38
10	5.14	0.90	51.93	7.15	1.90	39.38

These results indicate that there is an optimum level of Indulin AT at around 2-3% for maintaining fine particle size.

At 5-10% there is evidence of flocculation after 24 hours, especially in CIPAC C, shown by increasing mean particle size values and a reduction in percentage less than 1 µm in size.

(b) Soluble concentrates of picoxystrobin

10% w/w SL formulations in NMP containing 1, 2 and 5% w/v lignin were prepared and dilutions analysed for particle size after 24 hours. Results are shown in Table 3.

Table 3: Picoxystrobin dilutions

Indulin AT % w/v	CIPAC A			CIPAC C		
	Mean	Median	%<1 µm	Mean	Median	%<1 µm
1	14.01	0.56	76.32	23.81	0.68	65.22
2	1.69	0.51	84.29	1.11	0.52	81.21
5	1.78	0.46	86.54	1.16	0.57	73.57

(c) Soluble concentrate of tebuconazole

A 10% w/v SL formulation in NMP was prepared containing 5% lignin. Dilutions after 24 hours gave the results shown in Table 4.

Table 4: Tebuconazole dilution

Indulin AT % w/v	CIPAC A			CIPAC C		
	Mean	Median	%<1 µm	Mean	Median	%<1 µm
5	0.36	0.35	100.00	0.37	0.36	100.00

(d) Soluble concentrate of cyproconazole

A 10% w/v SL formulation in NMP was prepared containing 5% lignin.

The results obtained are shown in Table 5.

Table 5: Cyproconazole dilution

Indulin AT % w/v	CIPAC A			CIPAC C		
	Mean	Median	%<1 µm	Mean	Median	%<1 µm
5	14.41	0.35	78.90	14.22	0.33	82.39

(e) Soluble concentrate of a picoxystrobin/cyproconazole mixture

An SL formulation of 12.5% w/v picoxystrobin and 5.0% w/v cyproconazole was prepared containing 8% w/v lignin. Dilution after 24 hours gave the results shown in Table 6.

Table 6: Picoxystrobin/cyproconazole dilution

Indulin AT % w/v	CIPAC A		
	Mean	Median	%<1 µm
8	3.50	0.46	80.33

EXAMPLE 2

This Example illustrates the use of alternative polar solvents for preparing the concentrated solutions of the invention and the use of other pesticides.

SL formulations containing 10% w/w active ingredient and 4% w/w Indulin AT were prepared using the active ingredients azoxystrobin, hexaconazole, cypermethrin and mesotrione with NMP as solvent. In addition, similar formulations of azoxystrobin were prepared with the following solvents: GBL, DMSO, THFA, ethyl acetate and 50% NMP/50% PEG 200.

Dilutions of these formulations (2500 ppm active ingredient in CIPAC C water) were tested by the method described in Example 1 with the results shown in Table 7.

Table 7: Alternative solvents

Solvent	Dilution quality after time (hours)							Sieve Retention (75µm)
	Init	0.5	1.0	2.0	3.0	6.0	24.0	
NMP	*	*	*	*	*	*	*	nil
GBL	*	*	*	*	*	*	*	nil
DMSO	*	*	*	*	*	*	*	nil
THFA	*	*	*	*	*	*	*	nil
EL	*	*	*	*	*	*	*	nil
NMP/PEG	*	*	*	*	*	*	*	nil

* Fine sub-micron particle suspension

These results show that all combinations of active ingredients and solvents gave satisfactory dilutions after 24 hours, any fine suspension passing a 75 μm sieve.

CLAIMS

1. A concentrated pesticidal solution which comprises one or more water-insoluble pesticides and lignin dissolved in a water miscible, polar solvent.

2. A concentrated pesticidal solution according to claim 1 in which the amount of pesticide or pesticides used is from 0.5 to 50% w/v.

3. A concentrated pesticidal solution according to claim 1 or 2 in which the pesticide is a strobilurin fungicide or a triazole fungicide or a mixture thereof.

4. A concentrated pesticidal solution according to claim 1 or 2 in which the pesticide is a fungicide selected from the group consisting of azoxystrobin, picoxystrobin, tebuconazole, cyproconazole, and picoxystrobin in admixture with cyproconazole.

5. A concentrated pesticidal solution according to any one of the preceding claims in which the amount of lignin used is in the weight ratio of from 1:10 to 1:1of lignin to pesticide.

6. A concentrated pesticidal solution according to any one of the preceding claims in which the polar solvent is selected from the group consisting of γ-butyrolactone, tetrahydrofurfuryl alcohol, ethyl lactate and *N*-methyl pyrrolidone.

7. A concentrated pesticidal solution according to any one of the preceding claims which includes a polymer stabiliser or anti-settling agent.

8. A concentrated pesticidal solution according to claim 7 in which the polymer stabiliser or antisettling agent is ethyl cellulose.

9. A concentrated pesticidal solution which comprises:
(a) from 1 to 30% w/v of one or more water-insoluble pesticides and
(b) lignin in the weight ratio of from 1:10 to 1:1 of component (a), both (a) and (b) being dissolved in a water miscible, polar solvent.

10. A concentrated pesticidal solution according to claim 9 which contains up to 0.5% w/v of another additive.

11. A method of combating or controlling an agricultural pest which comprises applying to the pest or to a locus thereof, a pesticidally effective amount of an aqueous dispersion prepared by dispersing in water a concentrated pesticidal solution according to the invention.

INTERNATIONAL SEARCH REPORT

PCT/GB 02/04656

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A01N25/02 A01N43/653 A01N43/54 A01N43/40
//(A01N43/653,25:02),(A01N43/54,43:653,25:02),(A01N43/40,43:653,25:02)

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 7 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)
WPI Data, PAJ, EPO-Internal, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	WO 92 10937 A (DOWELANCO) 9 July 1992 (1992-07-09) cited in the application page 1, line 3 - line 16 page 2, line 16 -page 3, line 10 page 3, line 31 -page 4, line 32 page 5, line 22 -page 10, line 26	1-11
Y	EP 0 052 313 A (MOBAY CHEMICAL CORP) 26 May 1982 (1982-05-26) page 7, line 1 -page 8, line 1 page 12, line 32 -page 13, line 26	1-11
Y	EP 0 300 691 A (CHINOIN GYOGYSZER ES VEGYESZET) 25 January 1989 (1989-01-25) page 4, line 11 - line 15 page 4, line 22 - line 31 page 5, line 46 - line 48	3,4

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
13 February 2003	28/02/2003

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL – 2280 HV Rijswijk Tel. (+31–70) 340–2040, Tx. 31 651 epo nl, Fax: (+31–70) 340–3016	Lamers, W

1

Form PCT/ISA/210 (second sheet) (July 1992)

INTERNATIONAL SEARCH REPORT

PCT/GB 02/04656

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
Y	GB 2 252 499 A (ALBRIGHT & WILSON) 12 August 1992 (1992-08-12) page 15, paragraph 2	1-11
A	DATABASE REGISTRY 'Online! CHEMICAL ABSTRACTS SERVICE, COLUMBUS, OHIO, US; retrieved from STN-INTERNATIONAL XP002231057 registry number 8068-05-1 chemical names	1-11
A	"BIOCHEMIKALIEN ORGANISCHE VERBINDUNGEN für die Forschung und DIAGNOSTIKA" 1991 , SIGMA CHEMIE GMBH XP002231056 page 566, entry I 6384 "INDULIN AT"	1-11
A	WO 98 23350 A (GEORGE NEIL ;DAWSON STEPHEN (GB); ZENECA LTD (GB); WOOD WILLIAM MA) 4 June 1998 (1998-06-04) page 4, line 25 -page 5, line 2	1-11
A	EP 1 139 756 A (NOVARTIS ERFIND VERWALT GMBH ;SYNGENTA PARTICIPATIONS AG (CH)) 10 October 2001 (2001-10-10) page 1 page 4, paragraph 2 -page 5, paragraph 1	1-11

1

INTERNATIONAL SEARCH REPORT

PCT/GB 02/04656

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9210937 A	09-07-1992	AU 1415092 A	22-07-1992
		BR 9106407 A	18-05-1993
		CA 2075920 A1	19-06-1992
		EP 0515679 A1	02-12-1992
		JP 5504362 T	08-07-1993
		WO 9210937 A1	09-07-1992
EP 0052313 A	26-05-1982	US 4348385 A	07-09-1982
		AR 229516 A1	15-09-1983
		AT 15747 T	15-10-1985
		AU 543845 B2	02-05-1985
		AU 7747081 A	27-05-1982
		BR 8107457 A	10-08-1982
		CA 1163191 A1	06-03-1984
		DE 3172450 D1	31-10-1985
		DK 507181 A	18-05-1982
		EP 0052313 A1	26-05-1982
		ES 8303025 A1	01-05-1983
		GR 78018 A1	26-09-1984
		JP 57109701 A	08-07-1982
		NZ 198962 A	03-02-1984
		PT 73944 A ,B	01-12-1981
		ZA 8107903 A	27-10-1982
EP 0300691 A	25-01-1989	HU 47367 A2	28-03-1989
		AT 72923 T	15-03-1992
		BR 8803563 A	08-02-1989
		CN 1036124 A ,B	11-10-1989
		DD 286097 A5	17-01-1991
		DE 3868751 D1	09-04-1992
		EP 0300691 A2	25-01-1989
		ES 2037835 T3	01-07-1993
		GR 3004781 T3	28-04-1993
		WO 8900380 A1	26-01-1989
		JP 1090106 A	06-04-1989
		KR 9609483 B1	20-07-1996
		PL 273756 A1	03-04-1989
		SU 1836011 A3	23-08-1993
		US 4943307 A	24-07-1990
GB 2252499 A	12-08-1992	AT 152318 T	15-05-1997
		AU 661835 B2	10-08-1995
		AU 1077492 A	13-08-1992
		BG 61496 B1	31-10-1997
		BR 9200395 A	13-10-1992
		CA 2060476 A1	09-08-1992
		CS 9200354 A3	16-09-1992
		CU 22361 B1	07-03-1995
		DE 69219373 D1	05-06-1997
		DE 69219373 T2	25-09-1997
		DK 498231 T3	03-11-1997
		EG 19577 A	30-09-1995
		EP 0498231 A1	12-08-1992
		ES 2103836 T3	01-10-1997
		FI 920530 A	09-08-1992
		GR 3024218 T3	31-10-1997
		HU 61432 A2	28-01-1993
		IE 920411 A1	12-08-1992

INTERNATIONAL SEARCH REPORT

PCT/GB 02/04656

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
GB 2252499 A		IL 100757 A	23-07-1996
		JP 3313128 B2	12-08-2002
		JP 4327503 A	17-11-1992
		KR 240291 B1	02-03-2000
		MX 9200546 A1	01-08-1992
		NO 920460 A ,B,	10-08-1992
		NZ 241510 A	26-08-1994
		PL 293410 A1	19-10-1992
		RO 110942 B1	30-05-1996
		SG 47549 A1	17-04-1998
		SK 280855 B6	14-08-2000
		TR 28696 A	16-01-1997
		US 5547918 A	20-08-1996
		ZA 9200548 A	30-12-1992
WO 9823350 A	04-06-1998	AT 204501 T	15-09-2001
		AU 4716997 A	22-06-1998
		BR 9714307 A	02-05-2000
		CN 1238708 A ,B	15-12-1999
		DE 69706312 D1	27-09-2001
		DE 69706312 T2	07-02-2002
		DK 946232 T3	08-10-2001
		EP 0946232 A1	06-10-1999
		ES 2163137 T3	16-01-2002
		WO 9823350 A1	04-06-1998
		JP 2001504758 T	10-04-2001
		US 6338742 B1	15-01-2002
EP 1139756 A	10-10-2001	EP 1139756 A1	10-10-2001
		AU 2097600 A	03-07-2000
		BR 9916268 A	04-09-2001
		JP 2002532395 T	02-10-2002
		US 2002040044 A1	04-04-2002
		WO 0035284 A1	22-06-2000